

IN THE SPECIFICATION:

A marked version of the following amended paragraphs is attached hereto as Exhibit A. Matter that has been deleted from the paragraph is indicated by brackets and matter that has been added to the paragraph is indicated by underlining. A clean version of the following amended paragraphs is attached hereto as Exhibit B.

Please amend the specification as follows:

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On page 49, please replace the paragraph beginning "According to the preferred method" with the following paragraph:

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C \ According to the preferred method, a residual distribution is constructed by repetitively solving Eqn. 5 with randomized input data and accumulating the residuals to form the empirical residual distribution. Thereby, the constructed empirical residual distribution arises from random data that has the same population statistics as the actual data. In detail, first, either the drug response data or the pathway response data (but not both) are randomized in step 505 with respect to the drug exposure levels or the perturbation control parameters, respectively. This randomization transformation is represented by the following transformation.

$$\begin{aligned} D_k(t_l) &\leftarrow D_k(t_{\Pi(l)}) \\ R_{i,k}(p_{i,l}) &\leftarrow R_{i,k}(p_{i,\Pi(l)}) \end{aligned} \tag{10}$$

In Eqn. 10,  $\Pi$  represents a perturbation independently chosen for each cellular constituent. Either the drug response or the each pathway response (but not both) is randomized according to Eqn. 10. Accordingly, the randomized drug or pathway response data are derived from the measured data by independent perturbations of the measurement points. Second, Eqn. 5 is then solved by the chosen numerical approximation technique in step 504 and the value of the resulting residual saved. These steps are repeated for enough randomizations to construct a sufficiently significant expected probability distribution of residuals. In order to obtain confidence levels of 99% or better (*i.e.*, a P-value less than 0.01), then more than 100 randomizations are needed.

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IN THE CLAIMS:

A marked version of the claims showing the amendments is attached hereto as Exhibit C. Matter that has been deleted from claims 41, 49, 80-83 and 85-87 is indicated by brackets